CONTRIBUTION TO THE STUDY OF BERIBERI.*

(Preliminary Note with some Conclusions.)

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Beriberi has been observed in Cuba on several occasions in epidemic form, as a result of conditions of depression and want, as, for instance, slavery, and the reconcentration of the rural population in the cities during the war of independence. There have been, on the other hand, cases that could not be connected with these causes.

It becomes every day more apparent, therefore, that we must differentiate between the essential form of beriberi, which is caused by starvation and which is a disease evidently akin to scurvy, and a true pseudo-beriberi, characterized by a polyneuritis similar anatomically with that of true beriberi, but differing in nature just as the epidemic anterior poliomyelitis differs from the affection produced by varied and well-known organisms.†

The cases recently observed by me in the Santa Clara jail were cases of acute beriberi in individuals accustomed to a fair and varied diet. The etiologic factor here was very virulent, since out of seven persons affected, four died with the striking phenomena of precordial angor, from cardiac dilatation, shown by the autopsy to have been very marked, and in one case accompanied with pericardial effusion to the amount of four hundred cubic centimeters.

Samples of the rice consumed in the jail showed it to be polished rice. A bacteriological study of these samples showed the presence of numerous spores capable of resisting the boiling temperature (100°C.) for twenty minutes. By the destruction in this wise of other saprophytic germs, the spores are left in pure culture. This highly amylolytic germ produces glucocides a few hours after the cooking of the rice. The germ produces also valerianic acid and probably butyric acid and low grade alcohols. These facts I consider important. The qualitative and quantitative analysis of these products is the subject of further investigations.

The spores in cooked rice are transformed in a few hours into long filaments which later form chains by dividing into sections three to five microns in length. This transformation into chains occurs in about two

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† Studies by Flexner.

days. Staining these forms by Gram, without washing in alcohol, they take the anilin dye completely, showing no amyloid reaction. On the third day or a little earlier, the elements take cigar-shaped, lanciform, or pipe-shaped forms such as are found in other diastastic bacteria described by Le Dantec in connection with certain organisms found in the feces of persons who died of beriberi. In their new form, the organisms give the amyloid reaction, with the exception of the new spore, which is generally at the end of the organism, and which takes the anilin dye, thus giving exactly the appearance of a lighted cigar.

The organism is essentially aerobic. This distinguishes it from other amylolytic organisms described as anaerobic by several authors. The resistance to heat above 80°C. distinguishes our organism from that of Le Dantec.

Boiled rice is the best culture medium. Damp rice sterilized under pressure is not a good culture medium, nor is any other amylaceous substance. Since the organism sporulates at once on agar, this is the best method of preserving cultures.

The liquid obtained from the cooking of this rice, in the proportion of one part of the grain to four of water, after boiling from fifteen to twenty minutes, becomes, from the first hours after the boiling, lethal to the rabbit and guinea-pig, when injected into the peritoneum in doses of sixteen cubic centimeters. These intraperitoneal injections cause death in from two and a half to six hours, and in almost all cases with the same symptoms. These begin half an hour after the injection and terminate with marked suffering from cardio-pulmonary symptoms.

The autopsies on the guinea-pigs always revealed dilatation of the right side of the heart, and sometimes of the left auricle; frequently also serous effusion in the pericardial and pleural sacs, as well as diffuse infiltration in extensive areas of the small intestines and the stomach; the peritoneum itself and other portions of the intestines remaining unaffected.

I have not yet made a study of the pneumogastric, phrenic, and diaphragmatic nerves, to disturbances of which I attribute the final symptoms. These are very similar to those encountered in acute beriberi of the cardio-pulmonary form.

Two other samples of rice from a different lot, obtained in Havana, and boiled in the same manner as above, and in which rice the spores and their derived forms could not be found, failed to produce any disturbances whatever, though the liquid was injected in larger doses, even to twenty cubic centimeters. I am sure that anaphylaxis has nothing to do with these phenomena. Doses of two, three, and four cubic centimeters, injected subcutaneously for many days, produced no immediate effects.

Special study is to be made of one case giving later manifestations. The same negative results have been obtained by intravenous injections in doses of two cubic centimeters.

The intradural injections are rapidly effective, especially if the cerebral substance be irritated by slight puncture. Very small doses of the rice water are then sufficient to cause death with the same manifestations as in those cases where injected in the peritoneal cavity.

The ingestion by the mouth gave no results in a guinea-pig fed for more than one month with rice which had been proven to be virulent by peritoneal injection. Doses of sixty, eighty, and more grams were thus given by the mouth without effect. No change was made in the ordinary feeding of the animals experimented upon. When the gastric mucous membrane was previously irritated, however, by administering six to eight cubic centimeters of water and alcohol, in equal parts, with three drops of hydrochloric acid for every ten of the mixture, and the animal allowed to recover completely from the manifestations of slight acute alcoholism, death was produced by the ingestion of ten cubic centimeters of the rice water, with the same symptoms as in the cases of peritoneal injections.

Do the experimental data above detailed warrant the assertion that the toxic substance produced in the infected rice acts solely by direct action upon the nerve elements? Is the previous irritation of the gastric mucosa necessary to set in motion this action through the digestive channel?

I have not been able yet to produce manifestations of chronic polyneuritis.

Without wishing to discuss, as yet, the phosphorus theory of the etiology of beriberi, I believe I am justified in pointing out the great analogy between the clinical facts and the experiments here detailed.

It has been my object, in presenting these notes before the American Public Health Association,* to stimulate, in the direction indicated, the studies on the etiology of beriberi in countries where the disease is pervalent, believing that the facts here recorded open the way to other and more complete experimental studies.

* December, 1911.